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Excipients used in the Formulation of Tablets

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Research Article

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ABSTRACT

Excipients are additive substances used in tablet formulation to improve bulkiness, disintegration, dissolution rate and bioavailability of the drug. The drug and excipient interaction study is carried using Infrared Spectrum to know the stability of excipients and drug.

INTRODUCTION

Excipients are inert substances used as diluents or vehicles for a drug. In the pharmaceutical industry it is a catch-all term which includes various sub-groups comprising diluents or fillers [1-9], binders or adhesives, disintegrants, lubricants, glidant, flavors, colors and sweeteners. All of these must meet certain criteria as follows [10-20]:

a) Physiologically inert.
b) Acceptable to regulatory agencies.
c) Physiologically and chemically stable.
d) Free from bacteria.
e) Should not interfere with the bioavailability of the drug.
f) Commercially available in the form and purity commensurate to pharmaceutical standards.
g) Low cost, inexpensive.
h) Meet the standards of regulatory requirements.

To assure that no excipient interferences with the utilization of the drug, the formulator must carefully and critically evaluate combinations of the drug with each of the contemplated excipients and must as certain compliance of each ingredient with existing standards and regulations. The screening of drug-excipient and excipient-excipient interactions carried out in pre formulation studies [21-30].

List of Excipients [31-40]

Diluents: Diluents are fillers used to make up the volume of tablet if tablet is inadequate to produce the volume. Diluents used as disintegrants in dispersible and orally disintegrating tablet.

Example: Lactose, Spray dried lactose, Micro crystalline cellulose (Avicel 101 and 102), Pvpk30 (Pearlitol SD200 and 25C), Sorbitol, Dibasic calcium phosphate dehydrate, Calcium sulphate dehydrate etc.

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Binders: Binders are used as binding agent in tablets; it provides cohesive strength to powdered materials. Binders are added in both dry and wet form to form granules.

Example: Gelatin, glucose, Lactose, cellulose derivatives-Methyl cellulose, Ethyl cellulose, Hydroxy propylmethyl cellulose,Hydroxy propyl cellulose, starch, Poly vinyl pyrrolidone (Povidone), Sodium alginate, Carboxymethylcellulose, Acacia etc.

Lubricants: Used to reduce the friction between die wall and tablet, prevent adhesion of tablet to dies and punches. Helps in easy ejection of tablets from die cavity. Classified in to 2 types.

Example: Insoluble- Stearic acid, Magnesium stearate, Calcium stearate, Talc, Paraffin.
Soluble- Sodium lauryl sulphate, Sodium benzoate, PEG 400, 600,8000 etc.

Glidants: Helps in free flowing of granules from hopper to die cavity. Minimize friction between particles.
Example: Colloidal Silicon dioxide (Aerosil), Cornstarch, Talc etc.

Anti-adherents: These are added to prevent adhesion of tablet material to punches and dies.
Example: Talc

Anti-adherent: Prevent sticking of tablet to dies and punches.

Superdisintegrants: When they come in contact with water in oral cavity/GIT break down in to small particles.
Example: Croscarmellose sodium (Ac-di-sol),Crospovidone (Polyplasdone), and Sodium starch glycollate, Starch etc.

Role of Super disintegrants in the manufacturing of tablets

Disintegrating agents are substances included in tablet formulations and in some hard shell capsule formulations to promote moisture penetration and dispersion of the matrix of the dosage form in dissolution fluids. An oral solid dosage form should ideally disperse into the primary particles from which it was prepared. Although various compounds have been proposed and evaluated as disintegrants, relatively few are in common usage today. Traditionally, starch has been the disintegrant of choice in tablet formulations, and it is still widely used. For instance, starch generally has to be present at levels greater than 5% to adversely affect compactibility, especially in direct compression. Moreover, intra granular starch in wet granulations is not as effective as dry starch [41-50].

Characteristics of disintegrant

The ideal disintegrant should have the following characteristics:
- Poor solubility
- Poor gel formation
- Good hydration capacity
- Good compressibility and flow properties
- No tendency to form complexes with the drugs

Factors affecting action of disintegrants

- Percentage of disintegrants present in the tablets.
- Types of substances present in the tablets.
- Combination of disintegrants.
- Presence of surfactants.
- Hardness of the tablets.
- Nature of Drug substances.

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- Mixing and Screening.

Classification of Superdisintegrants

1. Modified starches (Sodium starch glycolate, NF)
Description: Sodium carboxy methyl starch; the carboxy methyl groups induces hydrophilicity and cross-linking reduces solubility.
Trade name: Explotab®(Edward Mendell Co.), Primojel® Generichem Corp.), Tablo® (Blanver, Brazil)

2. Modified cellulose (Croscarmellose, NF)
Description: Sodium carboxymethyl cellulose which has been cross-linked to render the material insoluble.
Trade name: AcDiSol® (FMC Corp.), Nymcel ZSX® (Nyma, Netherlands), Primellose® (Avebe, Netherlands)

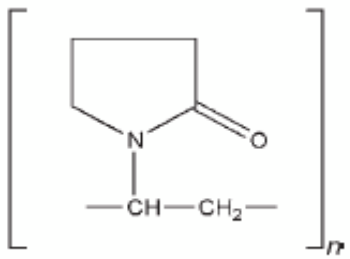
3. Cross-linked poly-vinyl pyrrolidone (Crospovidone, NF)
Description: Cross-linked poly vinyl pyrrolidone; cross-linking render the material insoluble in water.
Trade name: Crospovidone M® (BASF Corp.), Kollidon CL® (BASF Corp.)

4. Excipient profiles
PVP K30
Synonyms: E1201; Kollidon; Plasdone; poly [1-(2-oxo-1-pyrrolidinyl)ethylene]; polyvidone; polyvinylpyrrolidone; PVP; 1-vinyl-2-pyrrolidinone polymer.

Chemical Name and CAS Registry Number: 1-Ethenyl-2-pyrrolidinone homopolymer (9003-39-8)

Empirical Formula: (C6H9NO)n

Structural Formula:



Functional Category: Disintegrant; dissolution aid; suspending agent; tablet binder.

Applications:
Binders in wet granulation processes, coating agents suspending, stabilizing, or viscosity-increasing agent.

Typical Properties:

Acidity/alkalinity: pH = 3.0–7.0 (5% w/v aqueous solution).
Density (bulk): 0.29–0.39 g/cm3 for Plasdone.
Density (tapped): 0.39–0.54 g/cm3 for Plasdone.
Density (true): 1.180 g/cm3
Flowability: 20 g/s for povidone K-15;16 g/s for povidone K-29/32.

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Melting point: Softens at 1500C.
Moisture content: Hygroscopic.

Solubility
Freely soluble in acids, chloroform, ethanol (95%), ketones, methanol, and water; practically insoluble in ether, hydrocarbons, and mineral oil. In water, the concentration of a solution is limited only by the viscosity of the resulting solution, which is a function of the K-value.

Viscosity (dynamic)
The viscosity of aqueous povidone solutions depends on both the concentration and the molecular weight of the polymer employed. Viscosity (dynamic) is 5.5–8.5

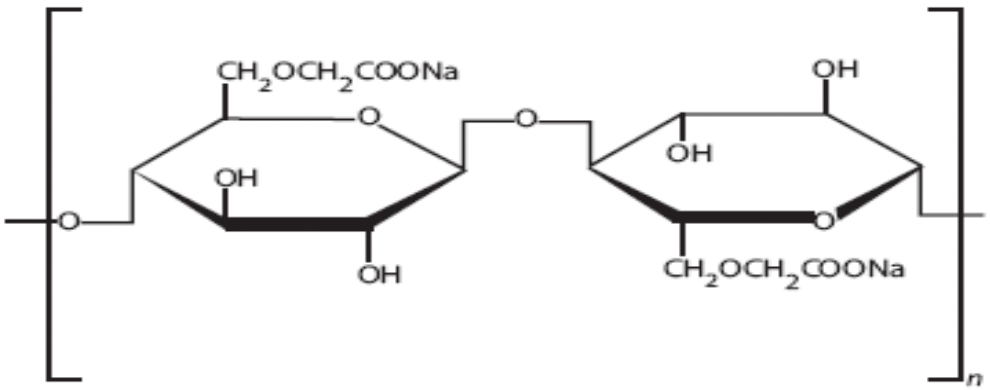
Stability and Storage Conditions
Povidone darkens to some extent on heating at 1508C, with a reduction in aqueous solubility. It is stable to a short cycle of heat exposure around 110–1308C.

Incompatibilities
Povidone is compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals [51-60].

CROSSCARMELLOSE SODIUM [61-70]

Synonyms: AC-Di-sol, cross linked carboxyl methylcellulose sodium, explocel.

XL-CMC



2. Description: It is odourless, white or greyish white powder.
3. Functional category: Tablet and capsule disintegrant.
4. Solubility: Insoluble in water.
5. Bulk density: 0.529 glcm3
6. Tapped density: 0.819 glcm3
7. Incompatibilities: Efficacy of crosscarmellose sodium may be slightly reduced in tablet formulations contain hygroscopic excipients such as sorbital.
8. Pharmaceutical applications: Disintengrant for capsules tablets & granules. In capsules it is used as a disintegrant in the concentration of 10 to 25% and tablets in the concentration of 0.5 to 5.0%.

CROSPOVIDONE [71-75]

1. Synonyms: cross linked povidone, kollidon CL, polyvinyl pyrrolidone

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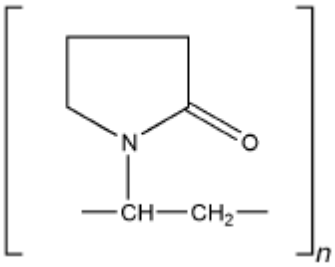
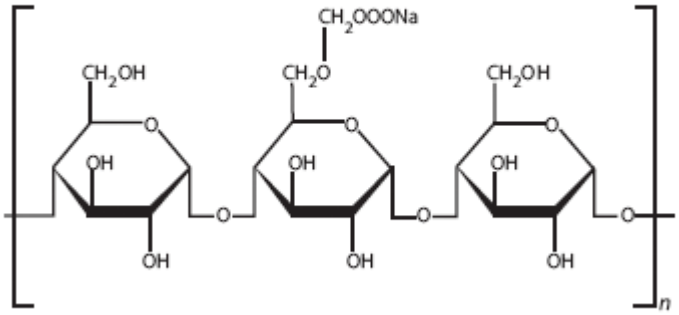
2. Structural Formula



3. Description: It is a white to creamy white, finely divided, free flowing practically taste less, odorless or nearly odorless hygroscopic powder
4. Functional category: Tablet disintegrants.
5. pH: 5.0 to 8.0.
6. Density: 1.22 gm/ cm3
7. Solubility: Practically insoluble in water and most common organic solvents.
8. Stability and storage conditions: Since crospovidone is hygroscopic, it should be stored in an air tight container in a cool, dry place.
9. Incompatibilities: Organic and inorganic pharmaceutical ingredients. When exposed to high water level, cross povidone may form molecular adduct with some materials.
10. Pharmaceutical applications: solubility enhancer [61-65].

SODIUM STARCH GLYCOLATE [76-85]
1. Synonyms: Sodium carboxy methyl starch, explotab, primojel

SSG



2. Description: It is white to off – white, odorless, tasteless, free flowing powder. It consists of oval or spherical granules.
3. Functional category: Tablet and capsule disintegrant
4. Solubility: Insoluble in organic solvents. Sparingly soluble in ethanol.
5. pH: 5.5 to 7.5
6. Stability and storage conditions: It is stable and it should be stored in well closed container to protect it from wide variations in humidity and temperature that may cause caking.
7. Pharmaceutical applications: oral pharmaceuticals as a disintegrant in capsule and tablet formulations in the concentration of 2 to 8%.

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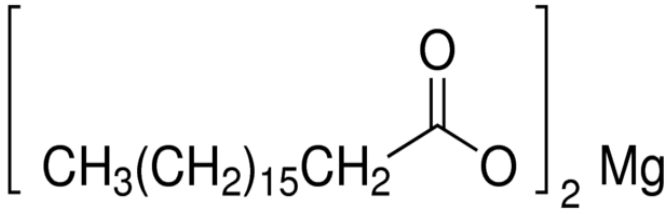
MAGNESIUM STEARATE [86-90]

1. Synonyms: Metallic stearate, Magnesium Salt.
2. Structural Formula: [CH3(CH2)16COO]2Mg



3. Description: Fine white, precipitated or milled, impalatable powder of low bulk density. Odor and taste are slight but characteristic. The powder is unctuous and readily adheres to skin.
4. Functional Category: Tablet or Capsule lubricant.
5. Solubility: Practically insoluble in water, alchohol, ethers. Slightly soluble in warm benzene and warm ethanol (95%).
6. Melting Point: 117°C to150°C
7. Stability and storage conditions: Stable and should be stored in a cool, dry place in a well closed container.
8. Incompatibilities: strong acids, alkalis and iron salts, strong oxidizing materials. Magnesium Stearate cannot be used in products containing aspirin, some vitamins and most alkaloidal salts.
9. Pharmaceutical applications: cosmetics, foods and pharmaceutical formulations. It is primarily used as a lubricant in capsule and tablet manufacture at concentration between 0.25 – 0.5% w/w.

AEROSIL [91-99]

1. Synonyms: Colloidal silica, aerosil, fumed silica, light anhydrous silicic acid.
2. Description: It is submicroscopic, light, loose, bluish-white, odorless, tasteless, non-gritty, amorphous powder.
3. Functional category: Glidant, suspending and / or viscosity increasing agent, anticaking agent.
4. PH: 3.3-4.4 (1 in 25 aqueous dispersion)
5. Solubility: Insoluble in purified water forms a colloidal dispersion. Soluble in hot solutions of alkali hydroxide. Insoluble in acids, except hydrofluoric acid.
6. Stability and storage conditions: Colloidal Silicon Dioxide is Hygroscopic, but absorbs large quantities of water without liquefying store in a well closed container.
7. Incompatibilities: Incompatible with diethylstilbestrol preparations.
8. Pharmaceutical applications:
• Drying agent for hygroscopic materials. Absorbent dispersing agent for liquids in powders or suppositories.
• Glidant and antiadherent in tabletting processes and encapsulation (0.1 – 0.5%)
• Thixotropic thickening and suspending agent in gels and semisolid preparations in the concentration of 2-10%.
• Emulsion stabilizer in the concentration of 1-5%.
• At the concentration of 0.5 to 2%, it is used in aerosols to promote particulate suspension.

CONCLUSION

This review may supply precious knowledge regarding the excipients which are additive substances used in tablet formulation to improve bulkiness, disintegration, dissolution rate and bioavailability of the drug.

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